DEPARTMENT OF DEFENSE

NEUROFIBROMATOSIS RESEARCH PROGRAM

FISCAL YEAR 2000

PROGRAM ANNOUNCEMENT

APRIL 7, 2000

U.S. Army Medical Research and Materiel Command
MCMR-PLF
1077 Patchel Street
Fort Detrick, Maryland 21702-5024

Table of Contents

Foreword

The U.S. Army Medical Research and Materiel Command (USAMRMC) has been directed by the Secretary of the Army to continue the Department of Defense (DOD) Neurofibromatosis Research Program (NFRP). The deadline, format, and other criteria specified for proposals in this NFRP Announcement are based on program objectives, public needs, and regulatory guidance.

General information on the USAMRMC can be obtained from the USAMRMC web site at http://mrmc-www.army.mil. Specific information on the DOD NFRP can be obtained from the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil. A copy of this Program Announcement and associated forms (except for the Proposal Cover Booklet; see Section 4 on the following page) also can be downloaded from the CDMRP web site at http://cdmrp.army.mil.

1. Inquiries

Questions concerning the preparation of proposals, formats, or required documentation can be addressed to the CDMRP at:

Phone: 301-619-7079
Fax: 301-619-7792
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP00-Program Announcement)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

Applicants should submit questions via e-mail or in writing regarding this program as early as possible. Every effort will be made to answer questions within 5 working days of receipt.

2. Research Involving Human Subjects and/or Human Anatomical Substances

All proposals submitted with research involving human subjects and/or human anatomical substances must be approved by the appropriate local review board. Proposals must also be approved by the U.S. Army Human Subjects Research Review Board (HSRRB). The HSRRB is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed and will require information in addition to that supplied to the local review board (see Appendix H). **All investigators submitting clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H before proposals are programmatically reviewed.**

Institutional Review Board (IRB) documentation from the primary submitting institution must be received no later than December 28, 2000 at 4:00 p.m. Eastern Time. This documentation may be submitted at the same time the proposal is submitted. If submitted after the proposal, send this documentation to:

Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP00-IRB)
1076 Patchel Street (Building 1076)
Fort Detrick, MD 21702-5024

3. Forms

Associated forms (except for the Proposal Cover Booklet; see Section 4 below) can be found in the Appendices of this Program Announcement and can be downloaded from the CDMRP web site at http://cdmrp.army.mil.

4. Proposal Cover Booklet (Bubble Sheet)

A Proposal Cover Booklet must be completed for each proposal according to the instructions found in Appendix C.

Proposal Cover Booklets can be requested via phone, fax, e-mail, or mail at the following addresses/numbers. Please allow sufficient time for delivery by regular mail.

Phone: 301-682-5501
Fax: 301-682-5521
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP00-Program Announcement)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

5. Proposal Submission

To be considered for an award submit the following documentation to the address at the end of this subsection:

Proposal: **ONE** clearly labeled original (binder-clipped) and **THIRTY** collated photocopies (stapled or binder-clipped) of the **entire package. Each copy must match the original including reprints of any publications.** Do not use rubber bands, or spiral or three-ring binders.

Proposal Cover Booklet:	**ONE** original (binder-clipped to the original proposal) and **THREE** photocopies (**not** binder-clipped to proposal copies).
Letters of Recommendation:	If required, binder-clipped to the front of the original proposal under the original Proposal Cover Booklet. See individual application instructions.
Abstract Pages:	**TWO** additional copies of both the technical and the public (nontechnical) abstracts in a manila clasp envelope along with a 3½" computer disk containing the abstract files (clearly labeled with the name of the principal investigator [PI], institution, and word processing program). Format abstracts in Word, WordPerfect, or ASCII.
Statement of Work:	**TWO** additional copies of the Statement of Work in the same manila clasp envelope with abstract copies and disk.
Packaging:	Package only **ONE** complete proposal submission (original plus all materials requested above) per box. If acknowledgment of proposal receipt is desired, enclose a self-addressed, stamped postcard with each submission. This postcard should state the proposal title and PI's name.
Noncompliance:	Noncompliance to established guidelines may be perceived as an attempt to gain an unfair competitive advantage and may therefore result in proposal rejection. Administrative reasons for **rejection** of all or part of proposals most frequently result from **failure to adhere to timelines, page limits, and font requirements.**
Send the Proposal to:	Commander U.S. Army Medical Research and Materiel Command ATTN: MCMR-PLF (NFRP00-Announcement) 1076 Patchel Street (Building 1076) Fort Detrick, MD 21702-5024

6. Receipt Deadlines

Deadlines for individual award mechanisms are provided in Item 9 (Timeline) on the following page and in the Reference Table of Award Mechanisms and Submission Requirements found on page vii.

Any proposal received by the USAMRMC after the exact date and time specified for receipt shall **not** be considered unless it is received before fiscal year 2000 award negotiations have been completed, and:

1. It was sent by mail, and it is determined by the Government that late receipt was due solely to mishandling by the Government after receipt at the Government installation, or

2. It was sent by U.S. Postal Service Express Mail Next Day Delivery, Post Office to the address listed in Section 5 on page iii (**do not use Second Day Delivery**) and postmarked no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline, or

3. It was placed into the control of a commercial courier service no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline for delivery by 4:00 p.m. Eastern Time on the due date, or

4. The Government, in its sole discretion, decides to accept the late proposal if it determines that no competitive advantage has been conferred and that the integrity of the competitive grants process will not be compromised.

Investigators are advised that documentation of time of receipt by the delivery agent may be necessary if a problem should occur.

7. Duplicate Submissions

Duplicate submissions of the same research project under different award mechanisms will **not** be allowed.

8. Previously Submitted Proposals

Resubmissions of previously reviewed proposals are acceptable. However, the applicant should be cautioned that the year-to-year status of funding for the NFRP does not permit the establishment of standing panels for peer review. Therefore, the resubmission of a revised proposal does not guarantee any funding advantage or an improved priority score. Resubmitted/ amended proposals should meet the requirements for the appropriate award category in the current Program Announcement and adhere to this year's format guidelines. Do not include summary statements of previously reviewed proposals.

9. Timeline

The timeline for all proposals is:

Letter of Intent (requested):	As soon as possible but no later than 2 weeks prior to the receipt deadline
Proposal Receipt Deadline:	**September 6, 2000 at 4:00 p.m. Eastern Time**
Peer Review:	November 2000

Request for RCQ[1] Documents:	As early as 2 weeks after the completion of peer review
IRB Documentation:	May be submitted at anytime but must be received no later than **December 28, 2000 at 4:00 p.m. Eastern Time**
Programmatic Review:	January 2001
Notification:	Approximately 2 weeks after the completion of programmatic review
Award Date:	No earlier than June 1, 2001 and no later than September 30, 2001

[1] Regulatory Compliance and Quality

Directions to Fort Detrick

From Washington, DC

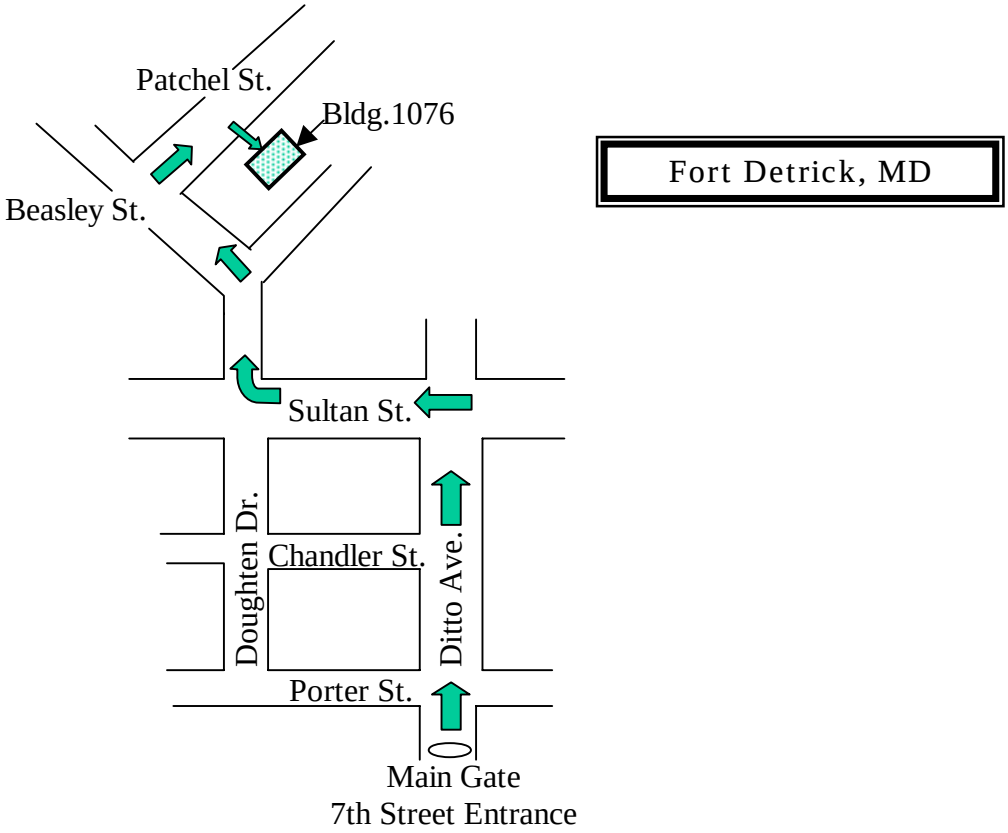
Take Interstate 495 to Interstate 270 North (exit #38) toward Rockville, Maryland. In Frederick, Interstate 270 ends and joins Route 15 North. Follow Route 15 North to the 7th Street exit. Turn right on 7th Street and proceed four blocks to Fort Detrick's Main Gate.

From Baltimore, MD

Take Interstate 695 to Interstate 70 West. In Frederick, take exit 53, Route 15 North. Follow Route 15 North to the 7th Street exit. Turn right on 7th Street and proceed four blocks to Fort Detrick's Main Gate.

Map of Fort Detrick

Packages to be delivered to the Neurofibromatosis Research Program must be delivered to building 1076 as shown on the map below. To gain entry to Fort Detrick, you will be required to show your driver's license at the Main Gate. **Please allow at least 15 minutes to pass through the gate area.**



Reference Table of Award Mechanisms and Submission Requirements

All investigators submitting clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H before proposals are programmatically reviewed. Therefore, IRB documentation from the primary submitting institution must be received no later than December 28, 2000 at 4:00 p.m. Eastern Time (ET).

Award Mechanism	Experience of PI	Key Mechanism Elements	Dollars Available	Receipt Deadline	Instructions for Proposal Preparation
Idea Awards	Independent investigators with all levels of experience	• Reward innovative and ideas technology • Support research on an issue relevant to NF • Preliminary data not required	An average of $100,000 per year in direct costs for a maximum of $200,000 over 2 years, plus indirect costs as appropriate	September 6, 2000 4:00 p.m. ET	Section III
New Investigator Awards	Independent investigators below the level of Associate Professor who have access to appropriate research facilities	• Reward innovative ideas and technology • Support research on an issue relevant to NF • Preliminary data not required	An average of $100,000 per year in direct costs for a maximum of $300,000 over 3 years, plus indirect costs as appropriate	September 6, 2000 4:00 p.m. ET	Section IV
Investigator-Initiated Research Awards (with or without Nested Postdoctoral Traineeship)	Independent investigators at a level equivalent to or above that of Assistant Professor Nested Postdoctoral Trainee: Recent doctoral graduates with 3 years or less of postdoctoral experience	• To sponsor basic research leading to clinical trials relevant to NF or drugs that can be introduced into clinical trials • To fund investigators and consortia across a broad spectrum of disciplines that are synergistic, nonexclusionary, and goal-focused • Preliminary data required	• No total dollar amount restrictions • Funding can be requested for up to 3 years • With Nested Postdoctoral Traineeship: a maximum of $49,000 per year inclusive of direct and indirect costs for a maximum of $147,000 per trainee over 3 years • No limit to the number of postdoctoral trainees nested under a given proposal	September 6, 2000 4:00 p.m. ET	Section V
Clinical Trial Awards	Investigators with clinical trial experience	• To sponsor Phase I or Phase II clinical trials of any novel therapeutic approach for NF type 1 and type 2 • Preliminary data required	• No total dollar amount restrictions • Funding can be requested for up to 3 years	September 6, 2000 4:00 p.m. ET	Section VI

I. Overview of the Congressionally Directed Medical Research Programs

I-A. History of the Congressionally Directed Medical Research Programs

Due to increased public awareness, the success of the Department of Defense (DOD) Congressionally Directed Medical Research Programs (CDMRP), and the work of grassroots advocacy organizations, Congress has appropriated monies directed toward specific diseases. Beginning in fiscal year 1992 (FY92), the U.S. Congress directed the DOD to manage various extra- and intramural grant programs targeted toward specific research initiatives. The U.S. Army Medical Research and Materiel Command (USAMRMC) established the CDMRP to administer these funds. To date, $1.5 billion has been targeted by Congress for research on breast, prostate, and ovarian cancer, neurofibromatosis, Defense women's health, osteoporosis, and other specified areas.

The CDMRP exists to support research that will positively impact the health of all Americans. The CDMRP strives to identify gaps in funding and provide award opportunities that will enhance program research objectives without duplicating existing funding opportunities. To meet these goals, the CDMRP has developed unique mechanisms to facilitate funding of quality research that addresses individual program objectives.

I-B. Investment Strategy

For each program, the CDMRP has developed and refined a flexible 7-year execution and management cycle that spans the development of an investment strategy through the completion of research. A Program Staff, composed of military and civilian scientists and clinicians, manages the CDMRP. For each program, an expert Integration Panel (IP) of scientists, clinicians, and consumer advocates is convened to deliberate issues and concerns unique to the program, establish an appropriate investment strategy, and perform programmatic review as described in Section I-C.2. Based upon this investment strategy, each program then uses a variety of award mechanisms to address the most urgent needs of the research community.

I-C. Proposal Evaluation

The CDMRP uses a two-tiered review process for proposal evaluation, which consists of scientific merit review and programmatic review, as recommended by the National Academy of Science's Institute of Medicine. The two tiers are fundamentally different. The first tier is a peer review of proposals against established criteria for determination of scientific merit. The second tier is a programmatic review of proposals that compares submissions to each other and recommends proposals for funding based on program goals.

I-C.1. Scientific Peer Review

Scientific peer review is conducted by panels organized by scientific discipline or specialty area. The primary responsibility of the scientific peer review panels is to provide unbiased, expert advice on the scientific and technical merit of proposals, based upon the review criteria developed for each award mechanism.

Each scientific review panel is composed of a chair, scientific reviewers, consumer reviewers, and a nonvoting executive secretary. The chair and scientific reviewers are recognized leaders in their fields. Selection of individuals as scientific reviewers is predicated upon their expertise as well as their varied levels of experience with scientific peer review. For the breast, prostate, and ovarian cancer research programs consumer reviewers are cancer survivors and representatives of consumer advocacy organizations; for the neurofibromatosis research program, consumer reviewers are individuals with neurofibromatosis or their family members and representatives of consumer advocacy organizations. Consumer reviewers are nominated by an advocacy organization and are selected on the basis of their leadership skills, commitment to advocacy, and interest in science. Consumers augment the scientific merit review by bringing the patient perspective to the assessment of science and to the relevance of research.

Panel members rate each proposal based on specific evaluation criteria developed for each award mechanism (see Sections III-B, IV-B, V-D, and VI-B). Two types of ratings are used. First, each of the evaluation criteria, except for the budget, is rated on a scale of 1 (lowest merit) to 10 (highest merit). This criteria scoring ensures that each component is considered in peer review. Second, the overall proposal is given a global score using a scale of 1 (highest merit) to 5 (lowest merit). Criteria scores are neither averaged nor mathematically manipulated to determine the global score. Instead, reviewers are asked to use the criteria scores as a guide in determining the global score. In rare instances, a proposal may be disapproved at scientific peer review if gravely hazardous or unethical procedures are involved, or if the proposal is so seriously flawed as to make its completion implausible.

The peer review summary statement is a product of scientific peer review. Each statement includes the investigator's technical and public (nontechnical) abstracts (verbatim), the peer review scores, and an evaluation of the project as assessed by the peer reviewers according to the evaluation criteria published in this Program Announcement. Summary statements assist investigators in assessing research projects and are forwarded to the next stage of the review process, programmatic review.

I-C.2. Programmatic Review

The second tier of the two-tiered review process is programmatic review. Programmatic review is accomplished by the IP, composed of scientists, clinicians, and consumer advocates. The scientific members of the IP represent many diverse disciplines and specialty areas and are experienced with peer review procedures. Consumer advocates represent national advocacy constituencies and are full voting members of the IP. With firsthand experience, consumer

advocates enhance the review process. One of the functions of the IP is to conduct programmatic review to obtain a broad portfolio of grants across all disciplines and recommend an investment strategy for appropriated funds.

Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool. IP members use the peer review summary statements, which include the proposal abstracts, to review proposals. The Statement of Work may also be reviewed at this level. However, the full proposal is not forwarded for programmatic review.

The IP is committed to funding a broad-based research portfolio. The ratings and recommendations of peer review panels are primary factors in programmatic review; the IP also must consider other criteria to establish this portfolio. The criteria the IP uses to make funding recommendations are:

- Ratings and recommendations of the peer review panels;
- Programmatic relevance;
- Relative innovation;
- Program portfolio balance with respect to research disciplines or specialty areas; and
- Other equitable factors, e.g., geographic distribution and adequate support for new investigators.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be recommended to the Commanding General, USAMRMC, for funding.

I-D. Notification

Following completion of the two-tiered evaluation process, every applicant will receive a letter indicating the funding status of their proposal, along with a scientific summary critique. The peer review summary statements will contain the criteria scores, the global score, and detailed comments that address the proposal's strengths and weaknesses with respect to each evaluation criterion. Notification letters will be sent as official information becomes available. Thus, not all investigators will be notified at the same time.

I-E. Annual and Final Reports

All awards will require the timely delivery of several reports during the research effort. These reports are necessary for the CDMRP to monitor progress.

The principal investigator (PI) should plan on a reporting requirement consisting of:

- an **annual** report (for each year of research except the final year) that presents a detailed summary of scientific issues and accomplishments; and

- a **final** report (submitted in the last year of the grant period) that details the findings and issues for the entire project.

All investigators are strongly encouraged to publish their results in scientific literature. All publications, abstracts, and presentations must cite the DOD as the source of the research funding. For example, "This research, under DAMD..., was supported by the Department of Defense Neurofibromatosis Research Program, which is managed by the U.S. Army Medical Research and Materiel Command." A PI must submit a copy of any manuscript or publication resulting from research to the CDMRP. In accordance with the Bayh-Dole Act (35 USC[1] 200 et seq.), title to inventions and patents resulting from such federally funded research may be held by the grantee or its collaborator, but the U.S. Government shall, at a minimum, retain nonexclusive rights for the use of such inventions. An investigator must contact the Contract Specialist and follow the instructions in the award document concerning license agreements and patents.

[1] United States Code

II. Department of Defense Neurofibromatosis Research Program

II-A. History of the Neurofibromatosis Research Program

The Department of Defense (DOD) Neurofibromatosis Research Program (NFRP) was established in fiscal year 1996 (FY96) to promote innovative, multi-institutional, multidisciplinary, and regionally focused research directed toward ameliorating neurofibromatosis. The DOD used the model established through recommendations from the Institute of Medicine for the U.S. Army Medical Research and Materiel Command's Breast Cancer Research Program (BCRP) to establish the NFRP. Like the BCRP, the NFRP employs a two-tiered scientific review process that funds meritorious research that will positively impact those living with neurofibromatosis (NF) type 1 or type 2. The program's success has encouraged Congress to appropriate additional funds to the NFRP in subsequent years, culminating in a $15M appropriation for the FY00 NFRP.

The program history of the FY96-99 NFRP is shown in Table II-1.

Table II-1: History of the DOD's Peer-Reviewed NFRP

Program History	FY96	FY97	FY98	FY99[2]
NFRP-Managed Appropriations for Peer-Reviewed Research	$8M	$8M	$9.8M	$11.5M
Number of Proposals Received	63	2	21	48
Number of Proposals Funded	10[1]	5[1]	9	22
Percentage of Applications Recommended for Funding	16%	100%	43%	46%
Number of Research Awards	10	3	9	22
Number of Infrastructure Awards	NA[3]	2	NA	NA

[1]Three FY96 Investigator-Initiated Research Award proposals on the alternate funding list were funded with FY97 monies.
[2]Award negotiations will not be finalized until September 2000.
[3]Not applicable as this type of award was not offered this FY.

II-B. Overview of the FY00 NFRP

Prospective applicants who are familiar with the Congressionally Directed Medical Research Programs (CDMRP) NFRP requirements from previous years are urged to review this Program Announcement carefully, as revisions to award mechanism definitions have been made.

The CDMRP, through this Program Announcement, is soliciting applications on NF research. The overall goal of this funding effort is to promote research that is directed toward improving the quality of life for individuals living with NF and their families.

The CDMRP is challenging the scientific community to design innovative NF research that will foster new directions, address neglected issues, and bring new investigators into the field. As in previous years, the central theme of the NFRP is innovation. Scientific ventures that represent under investigated avenues of research or novel applications of existing technologies are highly sought. Although the CDMRP wishes to encourage risk-taking research, such projects must, nonetheless, demonstrate solid scientific judgment and rationale.

Support for training of NF researchers, encouragement of established scientists in the field, and attraction of new scientific expertise from other fields are essential to the NF community. Proposals are sought across all areas of laboratory, clinical, behavioral, and epidemiological research including all disciplines within the basic, clinical, psychosocial, behavioral, sociocultural, and environmental sciences; nursing; occupational health; alternative therapies; public health and policy; and economics. Additionally, proposals that address the needs of minority, low-income, rural, and other underrepresented and/or medically underserved populations may be submitted from any eligible institutional source. Proposals are encouraged from investigators working at Historically Black Colleges and Universities and Minority Institutions.

II-C. FY00 Award Opportunities

The programmatic strategy for FY00 is to fund proposals from four mechanisms: (1) Idea Awards (Section III), (2) New Investigator Awards (Section IV), (3) Investigator-Initiated Research Awards (Section V) and (4) Clinical Trial Awards (Section VI). For the FY00 NFRP, approximately $12.4M[1] will be available to fund competitive peer-reviewed NF research.

Applicants may not submit the same proposal to more than one of these categories.

II-D. Participation of Juvenile Subjects

For proposals intending to recruit juvenile subjects, special attention must be paid to voluntary participation of juvenile subjects as described in Appendix H, part 5-a.

[1]A total of $15M was appropriated by Congress in FY00 to the DOD to continue the NFRP. Prior to receipt of these funds by the CDMRP, the DOD withholds approximately 8%-14% for Congressionally mandated and DOD initiatives. From the remaining funds, an additional 10% is set aside to manage the program, including costs for peer and programmatic review of proposals and the administration of grants/contracts throughout their entire period of performance (up to 7 years).

III. Idea Awards

III-A. Idea Awards

The intent of Idea Awards is to encourage innovative ideas and technology to neurofibromatosis (NF) research. These proposals may represent a new paradigm in the study of NF, challenge existing paradigms, or look at an existing problem from a new perspective. The proposed studies may be untested, but may present a high probability of revealing new avenues of investigation. Although this research is inherently risky in nature, the research plan must demonstrate solid scientific judgment and rationale. It is the responsibility of the investigator to clearly articulate how the proposed research is innovative.

Idea Award proposals are qualitatively different from traditional research proposals as outlined in Table III-1. Although Idea Award proposals do not require preliminary or pilot data, they should be based on a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning.

Table III-1: Differences between Traditional Research Proposals and Idea Research Proposals

Type of Proposal	Preliminary or Pilot Data	Research Approach
Traditional Research Proposal	Required	Expansion of well-established avenues of research
Idea Award Proposal	Not required (can be included if available)	Novel, challenging existing paradigms, high risk

Funding for Idea Awards can be requested for an average of $100,000 per year in direct costs for a maximum of $200,000 over 2 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, equipment, and travel to scientific meetings.

For complete proposal requirements, please refer to Section III-E. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections III-B and III-C.

III-B. Scientific Peer Review – Evaluation Criteria for Idea Award Proposals

Idea Award proposals will be evaluated according to the following criteria:

- **Research Strategy:** Are the conceptual framework, hypothesis, design, methods, and analyses adequately developed and well integrated to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative methods/tactics? Preliminary data are **not** required but may be included. If included, do the preliminary data

support the scientific rationale for the study? Does the investigator provide limited preliminary data or a clear-cut rationale supporting the research strategy?

- **Innovation:** Does the research employ novel concepts, approaches, or methods? Are the aims original and innovative? Does the project challenge existing paradigms, develop new methodologies or technologies, or address underexplored or unexplored areas?

- **Scientific Relevance:** Does this study address a critical problem in NF research? If the aims of the research are achieved, will the results be of benefit to the field of NF research or persons affected by the disease? Does the application make a convincing case for the relevance of the research to NF?

- **Applicant:** Does the applicant have a record of previous research experience, publications, and/or related professional training that indicates suitability for a research career? If the applicant is a previous Congressionally Directed Medical Research Programs (CDMRP) award recipient, what progress has been made in previous research endeavors? (See Appendix B, part 16.)

- **Environment:** Is the scientific environment an appropriate setting for the proposed research? Are the research requirements adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support?

- **Budget:** Is the budget reasonable for the research proposed? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

III-C. Programmatic Review – Evaluation Criteria for Idea Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. For example, How will the proposal contribute to the program's goal of improving the quality of life for individuals with NF and their family members? Will the project lead to new insights into the treatment of NF? Does the proposal meet the intent of the Idea Award mechanism? Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

III-D. Letter of Intent

All applicants considering submission of a proposal in response to this Program Announcement are requested to submit a "Letter of Intent" no later than 2 weeks prior to the receipt deadline. This form can be found in Appendix A and submitted as directed, or completed and submitted via the CDMRP web site at http://cdmrp.army.mil/?/announce/forms.

III-E. Proposal Preparation

Instructions for proposal preparation are found in Appendix B of this Program Announcement. The following proposal preparation information is specific for Idea Awards. Please note that the body of the proposal is limited to 10 pages, inclusive of figures, tables, and graphs and that the **receipt deadline is September 6, 2000 at 4:00 p.m. Eastern Time.**

1. Who May Apply – See Appendix B, part 1.

2. Proposal Acceptance Criteria – See Appendix B, part 2.

3. Proposal Cover Booklet – See Appendix B, part 3 and Appendix C.

4. Peer Review Referral Page – See Appendix B, part 4.

5. Proposal Title Page – See Appendix B, part 5.

6. Table of Contents – Use the table of contents found at the end of this section in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page. The DOD Neurofibromatosis Research Program recommends that applicants use this table of contents as a guide for assembling all required components of the proposal.

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
    In addition to the instructions found in Appendix B, part 10, Idea Award applicants should state explicitly how the proposed work is innovative and relevant to NF. Articulate how the combination of innovation and relevance in the proposal will impact and further programmatic goals.

11. Proposal Body – See Appendix B, part 11.
    The body of Idea Award proposals is limited to 10 pages. Figures, tables, and graphs, if used, must be included within this section. If color figures are submitted, it is recommended that they be provided in all copies to ensure their availability to all peer reviewers.

    For Idea Award proposals, it is the responsibility of the applicant to clearly articulate how the proposed research is innovative. The inclusion of preliminary data is **not** required, however, investigators must demonstrate a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning.

Describe the proposed project using the general outline provided below:

a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to this proposal. Cite relevant literature references.

b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

c. Objectives: State concisely the specific aims and the research strategy of the study.

d. Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. CDMRP-Sponsored Research Progress Report – See Appendix B, part 16.

17. Facilities/Equipment Description – See Appendix B, part 17.

18. Administrative Documentation – See Appendix B, part 18.

19. Detailed Cost Estimate – See Appendix B, part 19.
    Funding for Idea Awards can be requested for an average of $100,000 per year in direct costs for a maximum of $200,000 over 2 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, equipment, and travel to scientific meetings. The amount allotted for travel is $1,800 per year to attend scientific/ technical meetings.

20. Instruments – See Appendix B, part 20.

21. Publications and Patent Abstracts – See Appendix B, part 21.

22. Proposal Submission – See Appendix B, part 22.

23. Receipt Deadline – See Appendix B, part 23.
    Please note that the receipt deadline for Idea Award proposals is September 6, 2000 at 4:00 p.m. Eastern Time.

24. Institutional Review Board (IRB) Documentation – See Appendix B, part 24.
    All investigators submitting clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H before proposals are programmatically reviewed. Therefore, IRB documentation from the primary submitting institution must be received no later than **December 28, 2000 at 4:00 p.m. Eastern Time.**

25. Regulatory Compliance and Quality Requirements – See Appendix B, part 25.

Principal Investigator:_____

Proposal Title:_____

_____

Idea Award Proposal
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Page Number

IV. New Investigator Awards

IV-A. New Investigator Awards

The intent of New Investigator Awards is to promote and reward innovative ideas and technology from investigators in the early phases of their careers as well as those investigators new to neurofibromatosis (NF) research who have little or no preliminary data in NF. A New Investigator is defined as an independent investigator below the level of Associate Professor with access to appropriate research facilities. It is the responsibility of the investigator to clearly articulate how the proposed research is innovative.

New Investigator proposals should represent the start of something new, creating or introducing a unique or unusual approach to the study of NF as outlined in Table IV-1. This research may represent a new paradigm, challenge existing paradigms, or look at an existing problem from a new perspective. The proposed studies may be untested but have a high probability of revealing new avenues of investigation. Although New Investigator Award proposals do not require preliminary or pilot data, they should be based on a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning.

Table IV-1: Differences between Traditional Research Proposals, Idea Research Proposals, and New Investigator Research Proposals

Type of Proposal	Preliminary or Pilot Data	Mechanism Purpose
Traditional Research Proposal	Required	Expansion of well-established avenues of research
Idea Award Proposal	Not required (can be included if available)	Novel, challenging existing paradigms, high risk
New Investigator Proposal	Not required (can be included if available)	To prepare new, independent investigators below the level of Associate Professor and attract investigators new to the NF field

Funding for New Investigator Awards can be requested for an average of $100,000 per year in direct costs for a maximum of $300,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, equipment, and travel to scientific meetings.

For complete proposal requirements, please refer to Section IV-E. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections IV-B and IV-C.

IV-B. Scientific Peer Review – Evaluation Criteria for New Investigator Award Proposals

New Investigator Award proposals will be evaluated according to the following criteria:

- **Research Strategy:** Are the conceptual framework, hypotheses, design, methods, and analyses adequately developed and well integrated to the aims of the project? Are they based on sound scientific rationale and logical reasoning? Does the applicant acknowledge potential problem areas and consider alternative tactics? (Preliminary data are not required but may be included.)

- **Innovation:** Does the research employ novel concepts, approaches, or methods? Are the aims original and innovative? Does the project challenge existing paradigms, develop new methodologies or technologies, or address underexplored or unexplored areas?

- **Relevance:** To what extent will the project, if successful, make an original and important contribution to the goal of advancing research in the NF field? Does this study address a critical problem in NF research? Does the proposal make a convincing case for the relevance of the research to NF?

- **Applicant:** Does the principal investigator (PI) show potential for contributing to the NF field? Is the proposed work appropriate to the experience level of the PI and other researchers (if any)? Is there appropriate representation from all the expertise areas needed to conduct the study successfully? If the applicant is a previous Congressionally Directed Medical Research Programs (CDMRP) award recipient, what progress has been made in previous research endeavors? (See Appendix B, part 16.)

- **Environment:** Is the scientific environment appropriate for the proposed research? Are the research requirements adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support?

- **Budget:** Is the budget reasonable for the research proposed? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

IV-C. Programmatic Review – Evaluation Criteria for New Investigator Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. For example, How will the proposal contribute to the program's goal of improving the quality of life for individuals with NF and their family members? Will the project lead to new insights into the treatment of NF?

Does the proposal meet the intent of the New Investigator Award mechanism? Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

IV-D. Letter of Intent

All applicants considering submission of a proposal in response to this Program Announcement are requested to submit a "Letter of Intent" no later than 2 weeks prior to the receipt deadline. This form can be found in Appendix A and submitted as directed, or completed and submitted via the CDMRP web site at http://cdmrp.army.mil/?/announce/forms.

IV-E. Proposal Preparation

Instructions for proposal preparation are found in Appendix B of this Program Announcement. The following proposal preparation information if specific for New Investigator Awards. Please note that the body of the proposal is limited to 15 pages, inclusive of figures, tables, and graphs and that the **receipt deadline is September 6, 2000 at 4:00 p.m. Eastern Time.**

1. Who May Apply – See Appendix B, part 1.
   Eligible applicants must be independent investigators below the level of Associate Professor with access to appropriate research facilities.

2. Proposal Acceptance Criteria – See Appendix B, part 2.

3. Proposal Cover Booklet – See Appendix B, part 3 and Appendix C.

4. Peer Review Referral Page – See Appendix B, part 4.

5. Proposal Title Page – See Appendix B, part 5.

6. Table of Contents – Use the table of contents found at the end of this section in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page. The DOD Neurofibromatosis Research Program recommends that applicants use this table of contents as a guide for assembling all required components of the proposal.

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
    In addition to the instructions found in Appendix B, part 10, New Investigator Award applicants should state explicitly how the proposed work is innovative and relevant to NF. Articulate how the combination of training and relevance in the proposal will prepare the candidate for a career in NF research.

11. Proposal Body – See Appendix B, part 11.
    The body of New Investigator Award proposals is limited to 15 pages. Figures, tables, and graphs, if used, must be included within this section. If color figures are submitted, it is recommended that they be provided in all copies to ensure their availability to all peer reviewers.

    For New Investigator Award proposals, it is the responsibility of the investigator to clearly articulate how the proposed research is innovative. The inclusion of preliminary data is **not** required, however, investigators must demonstrate a sound scientific rational established through a critical review and analysis of the literature and/or logical reasoning.

    Describe the proposed project using the general outline provided below:

    a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to this proposal. Cite relevant literature references.

    b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

    c. Objectives: State concisely the specific aims and the research strategy of the study.

    d. Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. CDMRP-Sponsored Research Progress Report – See Appendix B, part 16.

17. Facilities/Equipment Description – See Appendix B, part 17.

18. Administrative Documentation – See Appendix B, part 18.
    Provide the following administrative documentation in the proposal submission:

    - A form signed by the Department Chair, Dean, or equivalent official verifying that the applicant is an independent investigator below the level of Associate Professor with access to appropriate research facilities and therefore is an eligible applicant for this award type. Use the Statement of Eligibility form at the end of this section.

19. Detailed Cost Estimate – See Appendix B, part 19.
    Funding for New Investigator Awards can be requested for an average of $100,000 per year in direct costs for a maximum of $300,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, equipment, and travel to scientific meetings. The amount allotted for travel is $1,800 per year to attend scientific/ technical meetings.

20. Instruments – See Appendix B, part 20.

21. Publications and Patent Abstracts – See Appendix B, part 21.

22. Proposal Submission – See Appendix B, part 22.

23. Receipt Deadline – See Appendix B, part 23.
    Please note that the receipt deadline for New Investigator Award proposals is September 6, 2000 at 4:00 p.m. Eastern Time.

24. Institutional Review Board (IRB) Documentation – See Appendix B, part 24.
    All investigators submitting clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H before proposals are programmatically reviewed. IRB documentation from the primary submitting institution must be received no later than **December 28, 2000 at 4:00 p.m. Eastern Time.**

25. Regulatory Compliance and Quality Requirements – See Appendix B, part 25.

Principal Investigator:_____

Proposal Title:_____

_____

New Investigator Award Proposal
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Page Number

STATEMENT OF ELIGIBILITY

Applicant's Name:_____

Title of Proposal:_____

Applicant's Organization Name:_____

Applicant's Organization Location:_____

_____

Signature of Applicant:_____

STATEMENT OF ELIGIBILITY

For the purposes of the Department of Defense Congressionally Directed Medical Research Program's Neurofibromatosis Research Program New Investigator Award mechanism as outlined in the Program Announcement, the applicant fulfills all of the following criteria:

- Is an independent investigator;
- Is below the level of Associate Professor and;
- Has access to appropriate research facilities.

I, _____of
(printed name of Department Chair, Dean, or equivalent official)

_____
(printed name of institution)

attest that the above-named investigator fulfills the requirements to be considered for a New Investigator Award.

Signature of Official:_____ Date:_____

V. Investigator-Initiated Research Awards (with or without Nested Postdoctoral Traineeship Awards)

V-A. Investigator-Initiated Research Awards

The intent of Investigator-Initiated Research Awards (IIRAs) is to sponsor basic research leading to clinical trials relevant to neurofibromatosis (NF) or drugs that can be introduced into clinical trials. These grants are intended to fund independent investigators across a broad spectrum of disciplines. Investigators interested in establishing consortia that are synergistic, nonexclusionary, and goal-focused are also encouraged to apply. An IIRA investigator is defined as an independent investigator at a level equivalent to or above that of Assistant Professor.

All IIRA proposals must include preliminary data relevant to NF research and the proposed project.

V-B. IIRAs without Nested Postdoctoral Traineeship Award Proposals

IIRAs without Nested Postdoctoral Traineeship Award proposals should represent the start of something new, creating or introducing a unique or unusual approach to the study of NF. This research may represent a new paradigm, challenge existing paradigms, or look at an existing problem from a new perspective. It is the responsibility of the investigator to clearly articulate how the proposed research is innovative.

Although there are no total dollar amount restrictions to these awards, funding for IIRAs (either with or without Nested Postdoctoral Traineeships) can only be requested for up to 3 years. Direct costs can cover salary, expenses including research supplies, equipment, and travel to scientific meetings.

For complete proposal requirements, please refer to Section V-G. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections V-D and V-E.

V-C. IIRAs with Nested Postdoctoral Traineeship Award Proposals

Nested Postdoctoral Traineeships are being offered as an optional part of IIRA proposals. The intent of the Nested Postdoctoral Traineeships is to enable doctoral degree graduates to either extend ongoing research related to NF or broaden the scope of their research to include work relevant to NF under the guidance of a designated mentor who is participating in the proposal. It is expected that the training will provide a valuable opportunity to further develop the experience necessary to advance the trainee's research career in NF.

A trainee is defined as a postdoctoral student with limited postdoctoral experience, 3 years or less at the time of proposal submission. Eligible postdoctoral candidates must have successfully defended a doctoral thesis and completed all academic requirements at the time of award negotiations, which will occur between June 1 and September 30, 2001.

There is no limit to the number of postdoctoral traineeships that can be nested within a given IIRA proposal. These Nested Postdoctoral Traineeship Awards can only be obtained as part of the IIRA mechanism.

Applicants must submit a biographical sketch of no more than three pages for each trainee and include it in the biographical sketch section (see Appendix B, part 14). To Be Named trainees are acceptable for the proposal submission. For those proposals approved for funding, the U.S. Army Medical Research Acquisition Activity must be provided with the name and biographical sketch of each applicant for review and approval.

As stated in Section V-B, there are no total dollar amount restrictions on IIRA proposals but funding can only be requested for up to 3 years. However, for the Nested Postdoctoral Traineeship portion of IIRA proposals, funding can be requested for a maximum of $49,000 per year inclusive of direct and indirect costs for a maximum of $147,000 per trainee over 3 years. Direct costs can cover salary, stipends, seminars and courses, expenses including research supplies, equipment, and travel to scientific meetings. Expenses relevant to the traineeship should be listed under the "Other" category on the "Detailed Cost Estimate" form (see Appendix B, part 19).

For complete proposal requirements, please refer to Section V-G. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections V-D and V-E.

V-D. Scientific Peer Review – Evaluation Criteria for All IIRA Proposals

All IIRA proposals will be evaluated according to the following criteria:

- **Research Strategy:** Are the conceptual framework, hypotheses, design, methods, and analyses adequately developed and well integrated to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? Do the required preliminary data in NF research support the proposed project? Is the research proposal founded upon appropriate preliminary data?

- **Scientific Relevance:** To what extent will the project, if successful, make an original and important contribution to the goal of advancing research in the field? Does this study address a critical problem in NF research? Does the proposal make a convincing case for the relevance of the research to NF?

- **Principal Investigator (PI) and Staff:** Is the PI appropriately trained and well suited to carry out this work? Does the PI show potential for contribution to the NF field? Is the proposed work appropriate to the experience level of the PI and other researchers (if any)? Is appropriate expertise available to conduct the study successfully? If the applicant is a previous Congressionally Directed Medical Research Programs (CDMRP) award recipient, what progress has been made in previous research endeavors? (See Appendix B, part 16.) **For IIRAs with Nested Postdoctoral Traineeship Awards,** are the PI and other scientific personnel well qualified to conduct training for the trainee(s)? Is there a senior staff member who is identified and responsible for the trainee(s)?

- **Environment:** Is the scientific environment an appropriate setting for the proposed research? Are the research requirements adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support? **For IIRAs with Nested Postdoctoral Traineeship Awards,** is the research training properly structured and balanced to ensure that the trainee will acquire the knowledge and necessary skills relevant to the scientific area being studied?

- **Budget:** Is the budget reasonable for the research proposed? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

V-E. Programmatic Review – Evaluation Criteria for All IIRA Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. For example, How will the proposal contribute to the program's goal of improving the quality of life for individuals with NF and their family members? Will the project lead to new insights into the treatment of NF? Does the proposal meet the intent of the IIRA mechanism?

Specific programmatic interests include proposals that:

- Perform cellular and biochemical studies investigating how abnormal functions of the genes NF type 1 and type 2 lead to pathogenesis;

- Perform studies of normal functions of NF type 1 and type 2 proteins in a variety of cell types, not necessarily nor exclusively the disease target tissue;

- Expand the knowledge of the genes that contribute to NF beyond the Gap-related domain in NF type 1;

- Attempt to define the genetic and nongenetic factors that play a role in tumor formation, growth, and progression in NF type 1 and type 2 tumors;

- Focus on how NF type 1 and type 2 protein function or lack of function leads to pathogenesis;

- Study the effect of hormonal events that might correlate with known effects of puberty and pregnancy on tumor growth;

- Focus on the development of improved models for gene therapy, especially for NF type 2;

- Emphasize the use of existing model systems to test potential therapies;

- Develop new methods of imaging and measurement of lesions including new approaches to quantitation of dermal NF;

- Study the pathogenesis of pseudoarthrosis and bone abnormalities in NF type 1; and

- Address early childhood developmental, psychosocial, and cognitive aspects for NF type 1.

Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

V-F. Letter of Intent

All applicants considering submission of a proposal in response to this Program Announcement are requested to submit a "Letter of Intent" no later than 2 weeks prior to the receipt deadline. This form can be found in Appendix A and submitted as directed, or completed and submitted via the CDMRP web site at http://cdmrp.army.mil/?/announce/forms.

V-G. Proposal Preparation

Instructions for proposal preparation are found in Appendix B of this Program Announcement. The following proposal preparation information is specific for all IIRAs. Please note that the body of the proposal is limited to 20 pages, inclusive of figures, tables, and graphs and that the **receipt deadline is September 6, 2000 at 4:00 p.m. Eastern Time.**

1. Who May Apply – See Appendix B, part 1.
   Eligible applicants for Nested Postdoctoral Traineeship Awards are postdoctoral students with 3 years or less experience at the time of proposal submission. At the time of award negotiations, which will occur no earlier than June 1, 2001 and no later that September 30, 2001, an applicant must have successfully defended a doctoral thesis and completed all academic requirements.

2. Proposal Acceptance Criteria – See Appendix B, part 2.

3. Proposal Cover Booklet – See Appendix B, part 3 and Appendix C.

4. Peer Review Referral Page – See Appendix B, part 4.

5. Proposal Title Page – See Appendix B, part 5.

6. Table of Contents – Use the table of contents found at the end of this section in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page. The Department of Defense Neurofibromatosis Research Program recommends that applicants use this table of contents as a guide for assembling all required components of the proposal.

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
In addition to the instructions found in Appendix B, part 10, all IIRA applicants should state explicitly how the proposed work is innovative and relevant to NF. Articulate how the combination of innovation and relevance in the proposal will impact and further programmatic goals.

11. Proposal Body – See Appendix B, part 11.

    a. IIRA Proposal Body.
    The body of IIRA proposals is limited to 20 pages. Figures, tables, and graphs, if used, must be included within this section. If color figures are submitted, it is recommended that they be provided in all copies to ensure their availability to all peer reviewers.

    For IIRA proposals, it is the responsibility of the investigator to clearly articulate how the proposed research is innovative. The inclusion of preliminary data **is required** for IIRA proposals; investigators must submit promising and well-founded preliminary data relevant to NF and the proposed project.

    Describe the proposed project using the general outline provided below:

    i. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to this proposal. Cite relevant literature references.

    ii. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

    iii. Objectives: State concisely the specific aims of the study.

    iv. Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

b. Nested Postdoctoral Traineeship Award Proposal Body.
The body of the Nested Postdoctoral Traineeship Award proposal is limited to one page per trainee. Identify the staff member who is responsible for the trainee. Describe the research training in which the trainee will participate such as research, coursework, laboratory techniques, conferences, and journal clubs.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14.
Investigators must include a description of their experience in NF research as part of the biographical sketch. A biographical sketch of no more than three pages must be included in this section for each named trainee.

15. Existing/Pending Support – See Appendix B, part 15.

16. CDMRP-Sponsored Research Progress Report – See Appendix B, part 16.

17. Facilities/Equipment Description – See Appendix B, part 17.

18. Administrative Documentation – See Appendix B, part 18.
Provide the following administrative documentation in the proposal submission:

- If applicable, a form signed by the Department Chair, Dean, or equivalent official verifying that the nested postdoctoral trainee has or will have successfully completed a doctoral degree at the time of award negotiation, has completed all academic requirements, and has no more than 3 years of postdoctoral training and therefore is an eligible applicant for this award type. Use the Statement of Eligibility at the end of this section.

19. Detailed Cost Estimate – See Appendix B, part 19.
There are no total dollar amount restrictions for IIRA proposals but funding can only be requested for up to 3 years. Funding for Nested Postdoctoral Traineeships can be requested for a maximum of $49,000 per year inclusive of direct and indirect costs for a maximum of $147,000 per trainee over 3 years. Direct costs can cover salary, stipends, seminars and courses, expenses including research supplies, equipment, and travel to scientific meetings. The amount allotted for travel is $1,800 per year to attend scientific/technical meetings. The amount allotted for postdoctoral trainee travel is $1,500 per year to attend scientific/ technical meetings.

20. Instruments – See Appendix B, part 20.

21. Publications and Patent Abstracts – See Appendix B, part 21.

22. Proposal Submission – See Appendix B, part 22.

23. Receipt Deadline – See Appendix B, part 23.
Please note that the receipt deadline for all IIRA proposals is September 6, 2000 at 4:00 p.m. Eastern Time.

24. Institutional Review Board (IRB) Documentation – See Appendix B, part 24.
All investigators submitting clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H before proposals are programmatically reviewed. IRB documentation from the primary submitting institution must be received no later than **December 28, 2000 at 4:00 p.m. Eastern Time.**

25. Regulatory Compliance and Quality Requirements – See Appendix B, part 25.

Principal Investigator:_____

Proposal Title:_____

_____

Investigator-Initiated Research Award with or without
Nested Postdoctoral Traineeship Award Proposal
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Page Number

STATEMENT OF ELIGIBILITY

Applicant's Name:_____

Title of Proposal:_____

Applicant's Organization Name:_____

Applicant's Organization Location:_____

_____

Signature of Applicant:_____

STATEMENT OF ELIGIBILITY

For the purposes of the Department of Defense Congressionally Directed Medical Research Program's Neurofibromatosis Research Program Investigator-Initiated Research Award (IIRA) with a Nested Postdoctoral Traineeship mechanism as outlined in the Program Announcement, the applicant fulfills all of the following criteria:

- Has or will have successfully completed a doctoral thesis at the time of award negotiation;
- Has or will have completed all academic requirements at the time of award negotiation; and
- Has 3 years or less of postdoctoral experience.

I, _____ of
(printed name of Department Chair, Dean, or equivalent official)

_____
(printed name of institution)

attest that the above-named investigator fulfills the requirements to be considered for an IIRA with a Nested Postdoctoral Traineeship.

Signature of Official:_____ Date:_____

VI. Clinical Trial Awards

VI-A. Clinical Trial Awards

The intent of Clinical Trial Awards (CTAs) is to sponsor clinical pharmacologic or gene therapy studies that look at toxicities (Phase 1) or investigate the efficacy (Phase 2) of any novel therapeutic approach for neurofibromatosis (NF) type 1 or type 2. CTAs will support Phase 1 and Phase 2 clinical trials that are likely to have a major impact on the treatment of NF. Ultimately, the goal of the CTA mechanism is to sponsor novel research that will substantially improve today's approach to the treatment of NF. **Applicants must include preliminary data to support the feasibility of their hypotheses and approaches, along with a detailed plan to conduct a Phase 1 or 2 clinical trial during the course of the award.** A requirement for consideration will be the inclusion of a clear experimental and appropriately powered statistical plan to perform a prospective clinical trial and study.

There are no total dollar amount restrictions to these awards. Funding can be requested for up to 3 years. Clinical trials often require the collaboration of multiple centers to assure sufficient patient access. Proposals that involve such collaborations should describe the role of each collaborating center in the clinical trial. As noted in Appendix F, it is the policy of the Department of Defense (DOD) that the principal investigator (PI) possess the equipment needed to support the proposed research; requests for equipment will be considered only in rare cases. The focus of the CTA should be on the clinical trial and work leading to the clinical trial. Therefore, careful consideration will be given to the appropriate percentage of the budget that will be devoted to equipment/infrastructure.

For complete proposal requirements, please refer to Section VI-E. Additional guidance for proposal preparation may be gained by reviewing the peer and programmatic review criteria listed in Sections VI-B and VI-C.

VI-B. Scientific Peer Review – Evaluation Criteria for CTA Proposals

CTA proposals will be evaluated according to the following criteria:

- **Trial Design:** Are the conceptual framework, design, methods, and analyses adequately developed and well integrated, including laboratory and other preclinical evidence, to support the clinical feasibility and promise of the approach? Have the logistical aspects of the clinical trial been appropriately addressed? Does the applicant demonstrate sufficient patient accrual? Has the availability of subjects for the trial, the prospect of their participation, and the likelihood of subject attrition been addressed? Is the recruitment schedule reasonable?

- **Clinical Relevance and Impact:** Does the study address an important problem related to the treatment of NF? If the aims of the proposal are achieved, are they likely to have a substantial clinical impact?

- **Statistical Plan:** Is the design of the clinical trial sound and sufficiently well developed with the required statistical power to lead to significant results? Is a clear statistical plan, including sample size projections and power analysis, outlined in the proposal? Is the appropriate statistical expertise represented on the research team?

- **Applicant(s):** Does the principal investigator (PI) have expertise in NF and experience conducting clinical trials? Are the other scientific personnel well qualified to participate in the project? Is there representation from all the areas of expertise needed to conduct the clinical trial successfully? If the applicant(s) is a previous Congressionally Directed Medical Research Programs (CDMRP) award recipient, what progress has been made in previous research endeavors? (see Appendix B, part 16.)

- **Environment:** Is there an appropriate clinical setting and are institutional resources available to support the study at each participating center? Are there assurances that therapies to be used are available? Are letters of commitment included from participating centers? Are there plans to have consumer representatives interacting with the staff of the clinical trial?

- **Budget:** Is the budget reasonable for the research proposed? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

VI-C. Programmatic Review – Evaluation Criteria for CTA Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. For example, How will the proposal contribute to the program's goal of improving the quality of life for individuals with NF and their family members? Will the project lead to new insights into the treatment of NF? Does the proposal meet the intent of the CTA mechanism? Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

VI-D. Letter of Intent

All applicants considering submission of a proposal in response to this Program Announcement are requested to submit a "Letter of Intent" no later than 2 weeks prior to the receipt deadline. This form can be found in Appendix A and submitted as directed, or completed and submitted via the CDMRP web site at http://cdmrp.army.mil/?/announce/forms.

VI-E. Proposal Preparation

Instructions for proposal preparation are found in Appendix B of the Program Announcement. The following proposal preparation information is specific for CTAs. Please note that the body of the proposal is limited to 50 pages, inclusive of figures, tables, and graphs and that the **receipt deadline is September 6, 2000 at 4:00 p.m. Eastern Time**.

1. Who May Apply – See Appendix B, part 1.

2. Proposal Acceptance Criteria – See Appendix B, part 2.

3. Proposal Cover Booklet – See Appendix B, part 3 and Appendix C.

4. Peer Review Referral Page – See Appendix B, part 4.

5. Proposal Title Page – See Appendix B, part 5.

6. Table of Contents – Use the table of contents found at the end of this section in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page. The DOD Neurofibromatosis Research Program recommends that applicants use this table of contents as a guide for assembling all required components of the proposal.

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
    In addition to the instructions found in Appendix B, part 10, CTA applicants should state explicitly how the proposed work is innovative and relevant to NF. Articulate how the combination of innovation and relevance in the proposal will impact and further programmatic goals.

11. Proposal Body – See Appendix B, part 11.
    The body of Clinical Trial Award proposals is limited to 50 pages. Figures, tables, and graphs, if used, must be included within this section. If color figures are submitted, it is recommended that they be provided in all copies to ensure their availability to all peer reviewers.

    For CTA proposals, it is the responsibility of the investigator to clearly articulate how the proposed research is innovative. The inclusion of preliminary data **is required** for all CTA proposal submissions; investigators must submit promising and well-founded preliminary data relevant to NF and the proposed project.

    Describe the proposed project using the general outline below:

    a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to the proposal, provide an overview of the state of the science, and discuss the current status and relevance of the trial. Cite relevant literature references as appropriate.

b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

c. Objectives: State concisely the specific aims of the study.

d. Preliminary Studies: A presentation of the studies that led to the proposed clinical trial is required. Data from pilot studies and additional supporting data from other research that support the necessity, feasibility, and potentiality of the trial should also be provided.

e. Methodology:

1. Clinical Protocol:

i. Study design for the intervention(s) to be used.

ii. Discussion of the potential biases in the research protocol and how they will be addressed.

iii. Description of clinical, behavioral, laboratory, and physiological tests and protocols.

iv. Patient recruitment:

iv-a. Inclusion and exclusion criteria.

iv-b. Description of the criteria to be used for assignment of patients to experimental conditions, methods of randomization (if any), and study endpoints.

iv-c. Availability of patients.

iv-d. Characteristics and appropriateness of the study population.

iv-e. Approaches to be utilized for recruitment, retention, and follow-up.

iv-f. Plans for maintaining the cooperation of subjects and addressing composition changes in the study population over the course of the trial.

iv-g. Data supporting recruitment and retention estimates.

iv-h. Ability of clinical centers to recruit and retain the proposed number of subjects.

v. Data management/quality control/data analysis:

v-a. Approach to data management.

v-b. Statistical plan including sample size calculations.

v-c. Methods for monitoring quality and consistency of the intervention(s) and data collection.

vi. Description of the methods of analysis (primary and secondary endpoints should be clearly defined and related to the power calculation).

vii. Human Subjects: The applicant should address any issues that may lead to concern for the welfare of subjects. The investigator must also address data security measures and confidentiality.

viii. Study organization/administration: A description of how the study will be organized and managed must be provided. Additionally, the following descriptions also must be included in the proposal body:

viii-a. Organizational chart showing the interactions between the PI, key personnel, and consumer representatives.

viii-b. Coordination of all participating centers.

viii-c. A timetable for completion of the various stages of the proposed clinical trial.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14.
Investigators must include a description of their experience in NF research as part of the biographical sketch. A biographical sketch of no more than three pages must be included in this section for each staff member or collaborator.

15. Existing/Pending Support – See Appendix B, part 15.

16. CDMRP-Sponsored Research Progress Report – See Appendix B, part 16.

17. Facilities/Equipment Description – See Appendix B, part 17.
Clinical, data management, and laboratory facilities, as well as required equipment should be described in detail for **all** participating institutions.

18. Administrative Documentation – See Appendix B, part 18.
Documentation of commitment from collaborating centers and institutions should be included in this section.

19. Detailed Cost Estimate – See Appendix B, part 19.
    There are no total dollar amount restrictions for CTA proposals but funding can only be requested for 3 years. A budget for the entire trial and data analysis period must be provided. If some costs of the trial are to be funded through other sources, provide detailed information about these sources. Budgets should clearly delineate which portions are being requested for support by this program and which are to be supported by other sources. A total overall budget as well as itemized, individual budgets for each year of support requested must be prepared. If multiple centers are proposed or if any subcontract(s) for personnel or facilities exist, separate itemized budgets must be prepared for each year of the study. Direct costs can cover salary, expenses including research supplies, and travel to scientific meetings. The amount allotted for travel is $1,800 per year, per PI, to attend scientific/technical meetings.

20. Instruments – See Appendix B, part 20.
    Please note that for CTA submissions, the clinical protocol must be included in the body of the proposal and not under the Instruments section.

21. Publications and Patent Abstracts – See Appendix B, part 21.

22. Proposal Submission – See Appendix B, part 22.

23. Receipt Deadline – See Appendix B, part 23.
    Please note that the receipt deadline for CTA proposals is September 6, 2000 at 4:00 p.m. Eastern Time.

24. Institutional Review Board (IRB) Documentation – See Appendix B, part 24.
    All investigators submitting clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H before proposals are programmatically reviewed. IRB documentation from the primary submitting institution must be received no later than **December 28, 2000 at 4:00 p.m. Eastern Time.**

25. Regulatory Compliance and Quality – See Appendix B, part 25.

Principal Investigator:_____

Proposal Title:_____

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Clinical Trial Award Proposal
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